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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,658	05/30/2001	Barbara P. Wallner	10248/7014	3397

Elizabeth R Plumer
Wolf Greenfield & Sacks
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210-2211

7590 03/24/2004

EXAMINER

RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/744,658

Applicant(s)

WALLNER, BARBARA P.

Examiner

Jeffrey E. Russel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,7-12,14-16,22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) 22 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,7-12 and 14-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 May 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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1. Applicant's election of the method and composition using the -B(D₁)(D₂) compounds of claim 7 in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 22 and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

2. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There is no antecedent basis in the claims for the phrase "the R group of proline" and "the R group of alanine" at claim 8, lines 3-4. There is no previous mention of proline or alanine or their R groups in the claims. It is also not clear what constitutes an R group of proline or alanine, and it is not clear if this R group is different than the R group used in the formula at claim 7, page 4, line 11.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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4. Claims 1, 7-10, 12, and 14-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 11-19, 31, and 36-81 of copending Application No. 09/578,363. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '363 application anticipate instant claims 1, 7-10, and 12. The '363 application claims treating colorectal cancer with an agent such as Val-boroPro (see, e.g., claims 7, 18, and 72), and colorectal cancer is an intestinal disease. With respect to instant claim 12, because the same active agent is being administered to the same subject by the same method steps in the claimed invention of the '363 application and the instant claimed invention, inherently the active agent in the claimed method of the '363 application will alter the substrate activity of the same substrates to the same extent claimed by Applicant. With respect to instant claims 14-16, while the '363 application does not claim oral or parenteral administration or a dosages of 0.01-100 mg/kg/day, it would have been obvious to one of ordinary skill in the art to determine all operable and optimal methods of administration and dosages for the active agents in the claimed method of the '363 application because method of administration and dosage are art-recognized result-effective variables which are routinely determined and optimized in the pharmaceutical arts.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claim 11 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 11-19, 31, and 36-81 of copending Application No. 09/578,363 in view of the Snow et al article (J. Am. Chem. Soc., Vol. 116, pages 10860-10869). The '363 application claims administering Val-boroPro, but does not claim

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administering this compound in cyclized form. The Snow et al article (see, e.g., the Abstract) teaches that boronic acid dipeptides, such as Val-boroPro, in aqueous solution are in equilibrium with their cyclized form. Therefore, inherently at least some cyclized Val-boroPro will be administered in the claimed method of the '363 application.

This is a provisional obviousness-type double patenting rejection.

6. Claims 1, 7-10, 12, and 14-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13, 15-29, 32-35, and 38-55 of copending Application No. 10/384,121. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '121 application anticipate instant claims 1, 7-10, and 12. The '121 application claims treating colorectal cancer with an agent such as Val-boroPro (see, e.g., claims 7 and 18), and colorectal cancer is an intestinal disease. With respect to instant claim 12, because the same active agent is being administered to the same subject by the same method steps in the claimed invention of the '121 application and the instant claimed invention, inherently the active agent in the claimed method of the '121 application will alter the substrate activity of the same substrates to the same extent claimed by Applicant. With respect to instant claims 14-16, while the '121 application does not claim oral or parenteral administration or a dosages of 0.01-100 mg/kg/day, it would have been obvious to one of ordinary skill in the art to determine all operable and optimal methods of administration and dosages for the active agents in the claimed method of the '121 application because method of administration and dosage are art-recognized result-effective variables which are routinely determined and optimized in the pharmaceutical arts.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claim 11 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13, 15-29, 32-35, and 38-55 of copending Application No. 10/384,121 in view of the Snow et al article (J. Am. Chem. Soc., Vol. 116, pages 10860-10869). The '121 application claims administering Val-boroPro, but does not claim administering this compound in cyclized form. The Snow et al article (see, e.g., the Abstract) teaches that boronic acid dipeptides, such as Val-boroPro, in aqueous solution are in equilibrium with their cyclized form. Therefore, inherently at least some cyclized Val-boroPro will be administered in the claimed method of the '121 application.

This is a provisional obviousness-type double patenting rejection.

8. Instant claims 1, 9-12, and 14-16 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/097,376 because the '376 application, under the test of 35 U.S.C. 112, first paragraph, discloses the instant claimed invention. Instant claims 7 and 8 are not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/097,376 because the '376 application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the compounds of instant claim 7 which comprise an $[X]_m$ group or which do not comprise a C=O group attached to the ring, and does not disclose the phosphonate groups of claim 7 in which J can be any number of C, H, O, S, or N atoms.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. *Joy Technologies Inc. v. Quigg*, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. *In re Hoeschele*, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. *In re Clinton*, 188 USPQ 365, 367 (CCPA 1976); *In re Thompson*, 192 USPQ 275, 277 (CCPA 1976).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 7 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Wallner et al (U.S. Patent Application Publication 2003/0158114). Wallner et al teach treating colorectal cancer with an agent such as Val-boroPro (see, e.g., claims 7 and 18), and colorectal cancer is an intestinal disease.

Wallner et al is available as prior art against instant claims 7 and 8 because instant claims 7 and 8 are not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/097,376 for the reasons set forth in paragraph 8 above, and because the disclosure of Wallner et al relied upon in the rejection is entitled under 35 U.S.C. 119(e) to

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the benefit of the filing date of its provisional application, 60/135,861 (see, e.g., claims 7 and 17 of the '861 provisional application).

11. Claims 1, 9, 12, and 15 are rejected under 35 U.S.C. 102(a) and claims 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 98/25644. The WO Patent Application '644 teaches co-administering GLP-2 with DPP-IV inhibitors in order to increase the mass and length, to promote the growth, and to enhance the function of the small and/or large intestine. In particular, the drug combination is used, e.g., to promote the healing and regrowth of injured, ulcerated, or inflamed intestinal mucosa, and to treat or prevent gastrointestinal disorders such as celiac disease, post-infectious villous atrophy, and short gut syndrome. Pro-boroPro is particularly preferred as a DPP-IV inhibitor. The compounds are administered subcutaneously or intravenously, i.e. parenterally. See, e.g., page 2, line 30 - page 3, line 10; page 4, lines 13-23; page 9, lines 35-36; and claims 7, 16, and 17.

12. Claim 11 is rejected under 35 U.S.C. 102(a) as being anticipated by the WO Patent Application 98/25644 as applied against claims 1, 7-9, 12, and 15 above, and further in view of the Snow et al article (J. Am. Chem. Soc., Vol. 116, pages 10860-10869). The WO Patent Application '644 teaches administering Pro-boroPro, but does not teach administering this compound in cyclized form. The Snow et al article (see, e.g., the Abstract) teaches that boronic acid dipeptides, such as Pro-boroPro, in aqueous solution are in equilibrium with their cyclized form. Therefore, inherently at least some cyclized Pro-boroPro will be administered in the method of the WO Patent Application '644.

13. Claim 10 is rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/25644 as applied against claims 1, 7-9, 12, and 15 above, and further in view of

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the Snow et al article (J. Am. Chem. Soc., Vol. 116, pages 10860-10869). The WO Patent Application '644 teaches administering DPP-IV inhibitors in general, but does not teach Val-boroPro specifically. The Snow et al article teaches Val-boroPro and Pro-boroPro to be very potent inhibitors of DPP-IV, and teaches that Val-boroPro may be expected to have greater in vivo activity because it cyclizes, i.e. deactivates, more slowly. See, e.g., the Abstract. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use Val-boroPro as the DPP-IV inhibitor required by the WO Patent Application '644, because the WO Patent Application '644 is not limited to any particular DPP-IV inhibitor, because the Snow et al article teaches Val-boroPro to be a very potent inhibitor of DPP-IV and the substitution of one functional equivalent for another is prima facie obvious, and because Val-boroPro would have been expected to have greater in vivo activity in view of the teachings of the Snow et al article.

14. Claim 14 is rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/25644 as applied against claims 1, 7-9, 12, and 15 above, and further in view of the WO Patent Application 93/08259. The WO Patent Application '644 does not teach oral administration of its DPP-IV inhibitor. The WO Patent Application '259 teaches Pro-boroPro to be a DPP-IV inhibitor and teaches that it can be administered orally. See, e.g., page 21, lines 4-15, and claim 6. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to administer the Pro-boroPro of the WO Patent Application '644 orally, because the WO Patent Application '259 teaches that such DPP-IV inhibitors can be administered orally and because a drug which is administered orally tends to have a better compliance rate than a drug which is administered parenterally.

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15. Claim 16 is rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/25644. Application of the WO Patent Application '644 is the same as in the above rejection of claims 1, 7-9, 12, and 15. The WO Patent Application '644 does not teach Applicant's claimed effective amounts for the DPP-IV inhibitor. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to determine an operable and optimal effective amounts for the DPP-IV inhibitor of the WO Patent Application '644 because effective amounts/dosages are art-recognized result-effective variables which are routinely determined and optimized in the pharmaceutical arts.

16. The rejections set forth in the previous Office action are withdrawn in view of the claim amendments filed February 26, 2004.

Robl et al (U.S. Patent Application Publication 2003/0199563 and U.S. Patent No. 6,548,529) are cited as art of interest, teaching the treatment of diabetes and related diseases such as atherosclerosis using drug combinations including DP4 inhibitors, i.e. DPP-IV inhibitors. See, e.g., claims 20 and 32 of Robl et al '563. However, these references are not prior art to the instant claims because the disclosure of Robl et al which is relevant to Applicant's claims is not disclosed in the priority document 60/127,745.

If a copy of a provisional application listed on the bottom portion of the accompanying Notice of References Cited (PTO-892) form is not included with this Office action and the PTO-892 has been annotated to indicate that the copy was not readily available, it is because the copy could not be readily obtained when the Office action was mailed. Should applicant desire a copy of such a provisional application, applicant should promptly request the copy from the Office of Public Records (OPR) in accordance with 37 CFR 1.14(a)(1)(iv), paying the required fee under

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37 CFR 1.19(b)(1). If a copy is ordered from OPR, the shortened statutory period for reply to this Office action will not be reset under MPEP § 710.06 unless applicant can demonstrate a substantial delay by the Office in fulfilling the order for the copy of the provisional application. Where the applicant has been notified on the PTO-892 that a copy of the provisional application is not readily available, the provision of MPEP § 707.05(a) that a copy of the cited reference will be automatically furnished without charge does not apply.

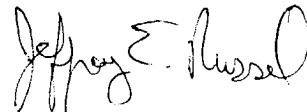
17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (571) 272-0961. The fax number for formal communications to be entered into the record is (703) 872-9306; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

A handwritten signature in black ink, appearing to read "Jeffrey E. Russel". The signature is fluid and cursive, with the first name "Jeffrey" and last name "Russel" clearly distinguishable.

Jeffrey E. Russel

Primary Patent Examiner

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JRussel

March 19, 2004